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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,051	04/03/2006	Giancarlo Tonon	02901/0203976-US0	5959
7278	7590	04/28/2008	EXAMINER	
DARBY & DARBY P.C.			LONG, SCOTT	
P.O. BOX 770			ART UNIT	
Church Street Station			PAPER NUMBER	
New York, NY 10008-0770			1633	
			MAIL DATE	DELIVERY MODE
			04/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/575,051	Applicant(s) TONON ET AL.	
	Examiner Scott D. Long	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 January 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18-27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The examiner acknowledges receipt of Applicant's Remarks and Claim amendments, filed on 29 January 2008.

Claim Status

Claims 28-40 are canceled. Claims 18-26 are amended. Claims 18-27 are under current examination.

Oath/Declaration

The new oath or declaration, having the signatures of all inventors, received on 1 February 2008 is in compliance with 37 CFR 1.63.

Priority

This application claims benefit as a 371 of PCT/IT04/00529 (filed 09/27/2004). The application claims benefit of foreign application ITALY MI2003A001909 (filed 10/03/2003). The instant application has been granted the benefit date, 3 October 2003, from the application ITALY MI2003A001909.

Response to Arguments - Claim Rejections 35 USC § 112

Response to Arguments – 35 USC 112, second paragraph

Applicant's arguments, see pages 5-6 and Claim amendments, filed 29 January 2008, with respect to claims 18-27 have been fully considered and are persuasive. The rejections of Claims 18-27 under 35 USC 112, second paragraph, have been made moot by the claim amendments submitted on 29 January 2008. Therefore, the examiner hereby withdraws the rejection of claims 18-27 under 35 USC 112, 2nd paragraph.

Response to Arguments - Claim Rejections 35 USC § 102/103

Applicant's arguments (Remarks, pages 6-8) filed 29 January 2008 have been fully considered and they are persuasive. The instant claims have been amended to change the scope of the instant claims. The rejections of claims 18-27 under 35 USC 102/103, have been made moot by the claim amendments submitted on 29 January 2008. Therefore, the examiner hereby withdraws the rejection of claims 18-27 under 35 USC 102/103 as anticipated/obvious over Fontana et al.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 18-27 are rejected under 35 U.S.C. 103(a) as being obvious over Schauer et al. (EP0752474, published 8/1/1997) in view of Fontana et al (Animal Cell Technology: Products from Cells, Cells as Products, 245-249. 1999).

Claim 18 is directed to a CHO cell deprived of a portion of the gene encoding for CMAH, wherein said portion comprises the sequence including and disposed between bases 787 and 1598 of cDNA encoding for CMHA. According to the specification, CMAH is CMP-NeuAc hydroxylase, which can be expanded to CMP-N-acetylneuraminic acid hydroxylase. The specification does not specifically describe the functionality

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encoded within of bases 787 and 1598 of the cDNA of CMAH; nor does the specification teach that deletion of this region alone is capable of eliminating CMAH activity from CHO cells. Fontana et al. abbreviate the CMP-N-acetylneuraminic acid hydroxylase gene as CNAH (page 245). Fontana et al. teach homologous recombination of CHO cells using a plasmid comprising DNA sequences coding for biologically active domains of CNAH. Schauer et al. teach production of CMP-N-acetylneuraminic acid hydroxylase-deficient cells (abstract), including CHO cells (page 6, line 29). Furthermore, Schauer et al teach, "the cells, which are deficient for hydroxylase activity are produced preferably by homologous recombination....For homologous recombination it is preferred to use a targeting vector" (page 6, lines 17-19) and "the targeting vector preferably contains about 5 to 10 kB of the genomic DNA sequence. This sequence may comprise introns and exons of the gene and may contain, in addition, 5'- or 3'-non-coding sequences. Preferably, genomic DNA from the cells to be mutated (e.g. CHO) is used." (page 6, lines 27-30). The examiner believes the teachings of Schauer et al. encompass 787 and 1598 of the cDNA of CMAH.

Claims 19-22 are directed to various deleted portions of the CMAH gene. Fontana et al. describe the Hampster CNAH cDNA sequence [with indications of exons and binding domains for CNAH and Cyt b5]; this portion of the CNHA cDNA encompassing the binding domains for CNAH and Cyt b5 found within amino acids 262 to 532 (claim 20). From what the examiner can decipher, it seems that the portions of the CMAH gene which encode binding domains for CMP-N-acetylneuraminic acid and for b5 cytochrome are suggested by Fontana et al. as important for deletion through

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homologous recombination in CHO cells. The examiner believes these teachings satisfy the limitations of claims 19-22. In addition, the examiner believes the genomic sequences described by Schauer et al. are obvious over the sequences recited in claims 18-22.

Claims 23 is obvious, since Fontana et al. teach “the aim of knocking-out the CNAH gene in CHO cells, for the production of recombinant glycoproteins devoid of NeuGc” because “NeuGc is potentially antigenic in man” (page 245). It would be important to knock-out both alleles to create a cell line that produces recombinant proteins devoid of NeuGc residues.

Claim 24-25 is directed to a CHO cell according to claim 15, wherein the portion eliminated has been replaced by at least one DNA sequence encoding for resistance to an antibiotic. Claim 25 further limits the antibiotic of claim 24 to zeocine. Fontana et al. teach “a replacement cassette...carrying the zeocin resistance gene” (page 247).

Claims 26-27 are directed to methods of expressing heterologous recombinant protein in CHO cells of claim 15, wherein said protein is at least one recombinant glycoconjugate. Fontana et al. teaches the goal of their method is “the production of recombinant glycoproteins” (page 245). Schauer et al. teach “production of recombinant proteins lacking N-glycoloylneuraminic acid side chains” (abstract).

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to make CHO cells which comprise a CMP-N-acetylneuraminic acid hydroxylase knock-out.

The person of ordinary skill in the art would have been motivated to make that modification to produce non-antigenic recombinant proteins useful for therapeutics in man, as suggested by both Schauer et al. and Fontana et al.

An artisan would have expected success, because both Schauer et al. and Fontana et al. produced non-antigenic recombinant proteins from CHO cells which comprise a CMP-N-acetylneuraminic acid hydroxylase knock-out.

Therefore the method as taught by Schauer et al. in view of Fontana et al. would have been *prima facie* obvious over the method of the instant application.

Conclusion

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**.

The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SDL/ Scott Long Patent Examiner, Art Unit 1633	/Janet L. Epps-Ford/ Primary Examiner, Art Unit 1633
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